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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/598,356	08/11/2008	**Kerstin Menander**	INGN:I20US	2981

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EXAMINER	
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ART UNIT	**PAPER NUMBER**
1632	
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03/04/2010	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/598,356	MENANDER ET AL.	
	Examiner	Art Unit	
	WU-CHENG Winston SHEN	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *1* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-30* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-30* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-30 are pending in the instant application and are subject to restriction in this office action.

Election/Restrictions

1. Restriction is required under 35 U.S.C. 121 and 372.

This application contains the following inventions or groups of inventions, which are not so linked as to form a single general inventive concept under PCT Rule 13.1.

In accordance with 37 CFR 1.499, applicant is required, in reply to this action, to elect a single invention to which the claims must be restricted.

I. Claims 1-3, 6-26, 29, and 30, drawn to a method of treating a subject with recurrent cancer comprising: (a) selecting a patient based on (i) prior treatment of cancer with first radiotherapy, and (ii) recurrence of cancer subsequent to said treatment, (b) administering to said subject an expression construct comprising a nucleic acid segment encoding p53, said segment under the control of a promoter active in a cancer cell of said subject, said expression construct expressing p53 in said cancer cell; and (c) subsequent to step (b), administering to said subject a second radiotherapy, whereby said expression construct sensitizes said cancer cell to said second radiotherapy, thereby treating said cancer.

II. Claims 1-5, 8-26, 29, and 30, drawn to a method of treating a subject with recurrent cancer comprising: (a) selecting a patient based on (i) prior treatment of cancer with first chemotherapy, and (ii) recurrence of cancer subsequent to said treatment, (b) administering to said subject an expression construct comprising a nucleic acid segment encoding p53, said segment under the control of a promoter

active in a cancer cell of said subject, said expression construct expressing p53 in said cancer cell; and (c) subsequent to step (b), administering to said subject a second chemotherapy, whereby said expression construct sensitizes said cancer cell to said second chemotherapy, thereby treating said cancer.

III. Claims 1-26, 29, and 30, drawn to a method of treating a subject with recurrent cancer comprising: (a) selecting a patient based on (i) prior treatment of cancer with a radiotherapy, and (ii) recurrence of cancer subsequent to said treatment, (b) administering to said subject an expression construct comprising a nucleic acid segment encoding p53, said segment under the control of a promoter active in a cancer cell of said subject, said expression construct expressing p53 in said cancer cell; and (c) subsequent to step (b), administering to said subject a chemotherapy, whereby said expression construct sensitizes said cancer cell to said chemotherapy, thereby treating said cancer.

IV. Claims 1-26, 29, and 30, drawn to a method of treating a subject with recurrent cancer comprising: (a) selecting a patient based on (i) prior treatment of cancer with a chemotherapy, and (ii) recurrence of cancer subsequent to said treatment, (b) administering to said subject an expression construct comprising a nucleic acid segment encoding p53, said segment under the control of a promoter active in a cancer cell of said subject, said expression construct expressing p53 in said cancer cell; and (c) subsequent to step (b), administering to said subject a radio-therapy, whereby said expression construct sensitizes said cancer cell to said radiotherapy, thereby treating said cancer.

V. Claims 1-3 and 6-30 drawn to a method of treating a subject with recurrent cancer comprising: (a) selecting a patient based on (i) prior treatment of cancer with surgery, and (ii) recurrence of cancer subsequent to said treatment, (b) administering to said subject an expression construct comprising a nucleic acid segment encoding p53, said segment under the control of a promoter active in a

cancer cell of said subject, said expression construct expressing p53 in said cancer cell; and (c) subsequent to step (b), administering to said subject a radiotherapy, whereby said expression construct sensitizes said cancer cell to said radiotherapy, thereby treating said cancer.

VI. Claims 1-5 and 8-30, drawn to a method of treating a subject with recurrent cancer comprising: (a) selecting a patient based on (i) prior treatment of cancer with surgery, and (ii) recurrence of cancer subsequent to said treatment, (b) administering to said subject an expression construct comprising a nucleic acid segment encoding p53, said segment under the control of a promoter active in a cancer cell of said subject, said expression construct expressing p53 in said cancer cell; and (c) subsequent to step (b), administering to said subject a chemotherapy, whereby said expression construct sensitizes said cancer cell to said chemotherapy, thereby treating said cancer.

2. The inventions listed as Groups I-VI do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons:

Applicant's claims encompass multiple inventions with multiple related but patentably distinct multiple methods (methods for treating a subject with recurrent cancer by p53 mediated gene therapy with various combinations of surgery, radiotherapy, and chemotherapy), and do not have a special technical feature which link the inventions one to the other, and lack unity of invention. The common technical feature in Groups I-VI is a step (b) recited in claim 1 regarding a method of treating s subject with recurrent cancer: administering to said subject an expression construct comprising a nucleic acid segment encoding p53, said segment under the control of a promoter active in a cancer cell of said subject, said expression construct expressing

p53 in said cancer cell. However, this common technical feature cannot be a special technical feature under PCT Rule 13.2 because the feature is shown in the prior art. For instance, **Roth et al.** teaches a retroviral vector containing the wild-type p53 gene under control of a beta-actin promoter was produced to mediate transfer of wild-type p53 into human non-small cell lung cancers by direct injection. Nine patients whose conventional treatments (i.e. surgery, radiotherapy, and chemotherapy) failed were entered into the study. Roth et al. teaches that no clinically significant vector-related toxic effects were noted up to five months after treatment. Roth et al. teaches that in situ hybridization and DNA polymerase chain reaction showed vector-p53 sequences in post-treatment biopsies, and apoptosis (programmed cell death) was more frequent in post-treatment biopsies than in pretreatment biopsies. Roth et al. teaches that tumor regression was noted in three patients, and tumor growth stabilized in three other patients (See Roth et al., Retrovirus-mediated wild-type p53 gene transfer to tumors of patients with lung cancer, *Nat. Med.* 2(9):985-91, 1996; This reference is cited as reference # C10 in the IDS filed by Applicant on 02/23/2007).

3. This application contains claims directed to more than one species of the generic invention. These species are deemed to lack unity of invention because they are not so linked as to form a single general inventive concept under PCT Rule 13.1.

The species are as follows:

(i) Claim 5: busulfan, chlorambucil, cisplatinum, carboplatinum, oxiplatin cyclophosphamide, dacarbazine, ifosfamide, mechlorethamine, melphalan, 5-FU, Ara-C, fludarabine, gemeitabine, methotrexate, doxorubiein, bleomycin, dactinomycin, daunorubicin,

idarubicin, mitomycin C, docetaxel, taxol, etoposide, paclitaxel, vinblastine, vincristine, vinorelbine, camptothecin, carmustinc, and lomustine. These are different species because each species is a different chemical with distinct structure and function for chemotherapy.

(ii) Claim 7: x-rays, gamma rays, or microwaves. These are different species because each species is a different type of radiation with a specific and distinct range of wavelengths and characteristics for radiotherapy.

(iii) Claim 8: brain cancer, head & neck cancer, esophageal cancer, tracheal cancer, lung cancer, liver cancer stomach cancer, colon cancer, pancreatic cancer, breast cancer, cervical cancer, uterine cancer, bladder cancer, prostate cancer, testicular cancer, skin cancer, rectal cancer lymphoma and leukemia. These are different species because each species is a different cancer occurred at a specific tissue with distinct underlying causes and potential treatments.

(iv) Claim 10: retroviral construct, a herpesviral construct, an adenoviral construct, an adeno-associated viral construct, or a vaccinia viral construct. These are different species because each species is a different viral vector with distinct nucleotide sequences, cloning capacity, and tropism for gene therapy.

(v) Claim 9 and 13: a viral expression vector (recited in claim 9) and a non-viral expression vector (recited in claim 13). These are different species because each species is a different type of vector with distinct nucleotide sequences of the construct, cloning capacity, and means for replication of the vector construct.

(vi) Claims 11 and 12: replication-competent viral expression vector (recited in claim 11) and replication-defective viral expression vector (recited in claim 12). These are different species

because each species is a different viral expression vector with distinct characteristics in term of capacity for replication.

(vii) Claim 15: CMV IE promoter, RSV LTR promoter, β-actin promoter, Ad-E1 promoter, Ad-E2 promoter and Ad-MLP promoter. These are different species because each species is a different promoter with distinct nucleotide sequences.

(viii) Claims 16-24: about 24 hours, about 2 days, about 3 days, about 7 days, about 14 days, about 1 month, about 2 months, about 3 months, and about 6 months. These are different species because each species is a different period of time between gene therapy and radiotherapy (or chemotherapy).

(ix) Claims 29 and 30: intratumoral, to a tumor vasculature, local to a tumor, regional to a tumor, and systemic (recited in claims 29 and 30). These are different species because each species is a distinct route of administration that requires different technical considerations regarding radiotherapy or chemotherapy.

Applicant is required, in reply to this action, to elect a single species, for each one of **(i)** to **(ix)** listed above, to which the claims shall be restricted if no generic claim is finally held to be allowable. The reply must also identify the claims readable on the elected species, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered non-responsive unless accompanied by an election. It is noted that the election of species must be consistent with the election of invention (i.e. restriction).

Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which are written in dependent form or otherwise include all the

limitations of an allowed generic claim as provided by 37 CFR 1.141. If claims are added after the election, applicant must indicate which are readable upon the elected species. MPEP § 809.02(a).

4. Because these inventions are independent or distinct for the reasons given above and there would be a serious burden on the examiner if restriction were not required because the inventions require a different field of search (see MPEP § 808.02), restriction for examination purposes as indicated is proper.

Applicant is advised that the reply to this requirement to be complete must include (i) an election of a species or invention to be examined even though the requirement be traversed (37 CFR 1.143) and (ii) identification of the claims encompassing the elected invention.

The election of an invention or species may be made with or without traverse. To reserve a right to petition, the election must be made with traverse. If the reply does not distinctly and specifically point out supposed errors in the restriction requirement, the election shall be treated as an election without traverse.

Should applicant traverse on the ground that the inventions or species are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the inventions or species to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C.103 (a) of the other invention.

5. Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Any inquiry concerning this communication from the examiner should be directed to Wu-Cheng Winston Shen whose telephone number is (571) 272-3157 and Fax number is 571-273-3157. The examiner can normally be reached on Monday through Friday from 8:00 AM to 4:30 PM. If attempts to reach the examiner by telephone are unsuccessful, the supervisory patent examiner, Peter Paras, Jr. can be reached on (571) 272-4517. The fax number for TC 1600 is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Wu-Cheng Winston Shen/
Patent Examiner
Art Unit 1632